Office Action Summary	Application No.	Applicant(s)
	10/583,977	KOPPELMAN ET AL.
	Examiner	Art Unit
	NORA ROONEY	1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 February 2011*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-22* is/are pending in the application.

4a) Of the above claim(s) *17-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 02/17/2011 has been entered.

2. Claims 17-22 are pending.

3. Claims 17-21 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03. Applicant's argument with respect to claims 17- 20 being withdrawn has been fully considered, but is not found persuasive. Claims 17-20 are directed to an in vitro method and the elected invention is an in vivo method. The Examiner has examined claims having to do with an in vivo method. If Applicant were to make claims 17-20 dependent upon the in vivo method, then they would be part of the elected invention. However, such is not the case so the claims are withdrawn. It is noted that methods of producing the protein are a separate invention because they have a separate status in the art, require separate searches and have different 112, first paragraph considerations.

4. Claims 21-22 are currently under consideration as they read on a method to desensitize a subject to an allergic reaction to 2S albumin comprising administering reduced and alkylated 2S albumin to the subject.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are

such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 21-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 02/074250 (IDS filed on 08/22/2006) in view of Bartolome et al. (PTO-892 mailed on 08/17/2010; Reference U) for the same reasons as set forth in the Office Action mailed on 08/17/2010.

WO 02/074250 teaches a method for treating an individual suffering from food allergy comprising administering to said individual a therapeutically effective amount of an allergen modified by reduction and alkylation wherein the allergen is brazil nut 2S albumin (In particular, page 3, line 24 to page 4, line 30, page 40, lines 1-29, Appendix 8, page 176, claims, whole document); wherein said reduction uses a reducing agent selected from the group consisting of 2-mercaptoethanol, dithiothreitol, dithioerythritol, and tributylphosphine (In particular, page 32, line 5-21); said alkylation uses an alkylating agent chosen selected from the group consisting of N-ethylmalimide, cystamine, iodoacetamide, and iodoacetic acid (In particular, page 32, lines 5-21); wherein administration induces production of Thelper-1 mediated subclasses of IgG antibodies (In particular, page 3, line 24 to page 4, line 30, page 40, lines 1-29, whole document); and results in down regulating the production of IgE antibodies (In particular, page 3, line 24 to page 4, line 30, page 40, lines 1-29, whole document).

Bartolome et al. teaches that 2S albumin Ber e 1 major allergen of Brazil nut is a sulfur-rich allergen having 8% cysteine that forms disulfide bonds which are important for its

conserved 2 S albumin structure. (In particular, page 136 right column) Ber e 1 is resistant to proteolytic digestion due to the disulfide bonds and the reference teaches that the stable structure allows the protein to reach and pass through the mucosal membrane of the intestine without complete enzymatic proteolytic degradation or acidic denaturation in the digestive tract, conferring its allergenic properties (In particular, last paragraph).

It would have been obvious to combine the specific teachings within the WO 02/074250 reference to arrive at the instantly claimed invention, particularly because Bartolome et al. teaches that the stable conformational structure of the Ber e 1 protein contributes to its allergenicity. It would have been obvious to alter the conformational structure of the Ber e 1 major allergen of Brazil nuts before administering the allergen to treat allergies to brazil nuts. WO 02/074250 specifically teaches how to alter the conformational structure of a protein due to disulfide bonds by reduction and alkylation to result in allergens, such as Ber e 1, with reduced IgE binding.

From the reference teachings, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the reference, especially in the absence of evidence to the contrary.

Applicant's arguments filed on 12/17/2010 have been fully considered, but are not found persuasive.

Applicant argues:

"The Office is of the view that Panacea teaches a method for treating an individual suffering from food allergy by administering a therapeutically effective amount of an allergen modified by reduction and alkylation wherein the allergen is Brazil nut 2S albumin. Respectfully, this is not an accurate statement of the teaching of Panacea. If it were, Panacea would destroy novelty of claims 21 and 22. Panacea at the cited sections on pages 3-4 and the section immediately prior thereto discusses getting rid of IgE binding sites which are putatively responsible for the allergenicity "by altering as little as a single amino acid within a protein..." or alternatively "disrupting one or more of the disulfide bonds that are present in the natural allergen." Reduction and alkylation is thus considered one possible option. The discussion in the cited section is completely generic and any application to a 2S albumin is based on the inclusion of 2S albumin in an extensive list of multiple allergens that occupies 15 pages of tables.

As pointed out in the previous Response, as the Examiner kindly recognizes, when a 2S albumin is illustrated in Panacea, it is modified by mutation not by reduction and alkylation. Therefore, a more accurate description of Panacea is that it teaches that one method to reduce allergenicity may be to reduce and alkylate the allergen or as an alternative to mutate an amino acid and also that 2S albumin is a known allergen.

Applicants appreciate that apparently the Office recognizes that this is the case since Bartolome is required to support the rejection. Bartolome concerns identifying the allergens from Brazil nut and concludes that 2S albumin is one of them. The Office states that Bartolome teaches that the particular 2S albumin of Brazil nut is resistant to proteolytic digestion and can pass through the mucosal membrane without proteolytic degradation or denaturation thus conferring allergic properties. Bartolome does say this, but the data obtained by Bartolome contradict any conclusion that reduction and alkylation of 2S albumin would result in lack of allergenicity, and Bartolome does not suggest that it would.

On the contrary, as noted by the Examiner, Panacea teaches that it is IgE binding properties that are responsible for allergenicity. Bartolome teaches on page 142, left-hand column, that immunoblotting assays in tricine SDS-PAGE under reducing conditions revealed the IgE binding capacity of both the large (9 kD) and small (3 kD) 2S albumin subunits.

Thus, rather than suggesting that this method would be successful in overcoming allergenicity, Bartolome specifically teaches that it would not. The subunits liberated by the reduction and alkylation are still allergenic in that they bind IgE.

Thus, Bartolome fails to make up for the deficiencies of Panacea, and this basis for rejection may be properly withdrawn."

It remains the Examiner's position that WO 02/074250 specifically teaches that allergens may be reduced and alkylated in order to disrupt one or more disulfide bonds that are present in the natural allergen and that Bartolome et al. teaches that 2S albumin Ber e 1 major allergens of Brazil nut is a sulfur-rich allergen having 8% cysteine that form disulfide bonds which are important for its conserved 2 S albumin structure. It would be obvious to disrupt the disulfide

bonds of the Ber e 1 protein from a combination of the teachings of the references and to administer the resulting allergen to treat brazil nut allergy.

Contrary to Applicant's assertion, the reference does not teach that allergenicity of the 2S albumin is not reduced under reducing conditions. Rather, the reference teaches that in one patient IgE binds to the subunits under reducing conditions. The reference does not teach whether or not the IgE binding capacity of the intact protein in non-reducing conditions is comparable to the IgE binding capacity of the two subunits particularly since it is noted that in Figure 4 the patient's serum is diluted 1:5 in the immunoblotting under non-reducing conditions. Further, the Bartolome reference is being relied on for its teaching that the stable conformational structure of Ber e 1 contributes to its allergenicity. The art of WO 02/074250 teaches that the allergens should be modified by reducing the disulfide bonds and alkylating the resultants, not just reducing the disulfide bonds alone. WO 02/074250 would is directed to a process of reducing and alkylating the allergens. As such, there is motivation to combine the references to result in the claimed invention.

8. No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nora M. Rooney whose telephone number is (571) 272-9937. The examiner can normally be reached Monday through Friday from 8:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by

telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

June 20, 2011

/Nora M Rooney/

Primary Examiner, Art Unit 1644